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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,352	01/14/2002	Renji Yang	0109015/024	4868

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,352	YANG ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,23-25,31-35,39-44,46,48-52,54-56,58-64,66,67 and 69-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,23-25,31-35,39-44,46,48-52,54-56,58-64,66,67 and 69-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/06 has been entered.

2. The rejection of claim 6 under 35 U.S.C. 102(b) as being anticipated by Nakafuka is withdrawn solely because of the amendment of the claims to "human neural precursor cell line"

3. Applicant's arguments filed 5/19/06 have been fully considered but they are not deemed to be persuasive.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 6, 23-25, 31-35, & 39-44, 46, 48-52, 54-56, 58-64, 66-67 & 69-77 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No: 20060104, and as follows.

In contrast to Applicants' assertions on pages 10-13 of the response, no proper antecedent basis or conception exists on pages 10, 19, 25, 11, 15, 10, 25-27, 14, 24, 3, 11 or in figure 1 for the broader concepts now or previously claimed. As previously made of record, it is improper to broaden what the specification actually discloses in order to create a new genus of claims after-the-fact; thereby, constituting new matter.

As far as Applicants' arguments that page 25-26 describe "interchangeability of ligand binding domains...", this is proper for only "glucocorticoid receptor, progesterone receptor, androgen receptors, vitamin D receptor, thyroid hormone receptors, retinoic acid receptors, and ecdysone receptor", in the presence of only "its appropriate ligands", as described, which are listed in the first paragraph of page 26 (i.e., as it relates to claims 49, 59 & 69). However, "a retinoid receptor", as claimed, is not the same as a "retinoic acid receptor; thereby, constituting new matter.

In contrast to Applicants' assertions, the broader concept of "wherein a portion of the cell line is capable of ..." has no proper antecedent basis or conception in context with that described on page 19 of the specification, similar to that previously made of record (i.e., as it now relates to claims **51**-56, 58-63, **64,** 66-67 & 69-71). Likewise, no where on page 10 of the specification (including the last sentence of the first paragraph and the first sentence of the second paragraph) does any proper antecedent basis or conception in context with that described within the specification at the time of filing the instant application exists for the new generic recitation of "resists differentiation in media containing a mitogen" (i.e., as it relates to claims **6, 23**-25, **31**-

35, 39-44, 46, 48-50, **51,** 52, 54-56, 58-63, **64**, 66-67, 69-71, **72** & 73-77); thereby, constituting new matter.

As previously made of record, any broader recitations of "receptor ligand-regulated c-myc gene" (e.g., as recited in claims 6, 23, 31, 51), for any generic and unknown "nuclear receptor" (i.e., as it relates to claims 48, 51 & 64), for "a c-myc *protein fused* with at least one nuclear receptor" (e.g., as it relates to claim 64), for "upon withdrawal of [any structurally undefined] mitogens" without also withdrawal of β-estradiol (e.g., see pg 18); thereby, still constituting new matter for the new and broader scope still recited in the claims. Lastly, the disclosure of a single species (i.e., MycER) obtained from someone else (i.e., Eiler et al) clearly does not provide proper basis for extrapolating to any "receptor ligand-regulated *c-myc* gene" construct, etc.; thereby, still constituting new matter.

As also previously made of record, no proper antecedent basis or conception exists in context with that described within the specification at the time of filing the instant application for the broader recitations of "wherein the second mitogen is different from the first mitogen" (i.e., as it relates to claims 40 & 58), for any generic "c-myc-activating agent", versus the previously recited Markush group (i.e., as it all relates to claims 31, 51, 64, 71 & 77); thereby, still constituting new matter.

Additionally, as previously made of record, no proper antecedent basis or conception exists in context with that described within the specification at the time of filing the instant application for the broader recitations of "wherein the culture includes a *monolayer* (versus feeder) component" (i.e., as it still relates to noncancelled claim 39), for "wherein *a portion* of the cell line is capable of differentiating into neurons" (i.e., as it relates to claim 64), for "at

least a *portion of* c-myc" (i.e., as it relates to claim 77), and for "includes a *clonal cell line*", versus that now recited in claims 62 & 63 (i.e., as it relates to claims 44, 46 & 73); thereby, constituting new matter.

Thus, Applicants' arguments are not persuasive.

6. Claims 6, 23-25, 31-35, & 39-44, 46, 48-52, 54-56, 58-64, 66-67 & 69-77 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No: 20060104, and as follows.

As previously made of record, no written description of any "c-myc ***gene***" with its structurally definable 5'- and 3'-flanking regions, etc. have been described within the instant specification. See again MPEP 2163, as it relates to written description for "genes".

7. Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

No antecedent basis now exists for "proto-oncogene" in base claim 72.

8. Claims 6, 23, 25, 31 & 33-35, 39-44, 46, 48-51, 54-57, 58-64, 66, 67 & 69-77 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nakafuka et al (IDS Ref #26), for the reasons made of record in Paper No: 20050124 & 20060104, and as follows.

In contrast to Applicants' as arguments on pages 13-14 of the response, and as previously made of record, the "portion" of Nakafuka's cells that *differentiate* into neurons occurs *only under conditions where "both* β-E2 and bFGF" *are present* (pg. 162, 2nd col), which appears similar to that disclosed on page 18 of the instant specification, and therefore, does not exclude Nakafuka's cells from being "***capable of*** differentiating into neurons upon withdrawal of [any] mitogen", including bFGF, if Nakafudk chose to do such. Nor does the recitation of "wherein the cell line resists differentiation when grown in medium contain **a** mitogen" exclude Nakafuka's cells, because intended use limitations do not change the structure of the product claimed. Thus, Applicants' arguments remain not on point with that currently claimed (i.e., a cell culture **product**) or with what Nakafuka et al actually teach; especially when Nakafuka et al teach *in vitro* stable cultures of rat/mammalian neural precursor cells transfected with the same *mycer* construct as used in the instant application, which is further recited in the instant claims; thereby, still being consistent with that held by the courts in *In re Thorpe, In re Marosi, Ex parte Gray, In re Best*, and *In re Brown* previously made of record.

In summary, Nakafuka et al teach *in vitro* stable monolayer and suspension clonal cultures of rat/mammalian neural precursor cells (which are at least initially cultured in the presence of unmodified cells/incomplete transfections) using the same *mycer* construct as used in the instant application (i.e., c-myc proto-oncogene cDNA construct fused to the ligand binding domain of an estrogen receptor selectable marker; pgs. 155, 156, 162 & Table 1; as it relates to

claims 6, 23, 31, 39, 43-46, 48-49, 51, 57, 59, 62-64 & 68-69); thereby, establishing the clonal cell line, MNS-57. These MNS-57 cells maintain a multipotential capacity to differentiate into neurons, astrocytes and oligodendrocytes/glial (e.g., pgs.153, 154, 159-160 & especially162 (2nd col.); as it relates to claims 23, 25 & 34-35). It is noted that the method of producing these cells using various mitogens, such as bFGF or EGF or β-E_2 (e.g., pgs 155-156 & 157-162) does not change the inherent properties of these claimed precursor/stem cell **products** (i.e., as it relates to claims 6, 31, 40, 51, 58, 60, 64 & 70-71); especially when CNS neural stem cells are inherently and naturally derived from pluripotent embryonic stem cells (i.e., as it relates to claims 25 & 33), and structurally and functionally possess the same inherent properties no matter what region within the brain from which they are derived (i.e., as it relates to claims 25, 33, 41-42, 50, 53-56 & 65-67); absence evidence to the contrary.

9. Claims 6, 23-25, 31-35, 39-44, 46, 48-52, 54-56, 58-64, 66-67 & 69-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakafuka et al (IDS Ref #26), in view of Eilers et al (IDS Ref #20) and/or Evans et al (1988), for the reasons made of record In Paper No: 20050124, and as follows.

In contrast to Applicants' arguments on page 14 of the response, as discussed above in *pp* #8, Applicants' arguments again are not on point with the pending rejection, or with the "**product" claimed**, and therefore, are not persuasive for the reasons made of record.

In summary, Nakafuka et al. is as described above. However, although Nakafuka et al. teach the importance of "understand[ing] the developmental processes of the [mammalian/

human] CNS" (pg. 153), they do not specifically teach a stable culture of human neural precursor cells.

Eilers et al. teach both the c-myc construct used above by Nakafuka et al., as well as a similar c-myc construct, *mycgr*, contains the sequence that encodes the hormone [ligand] - binding domain of the rat glucocorticoid receptor fused to the 3' end of *myc* transforms these cells in a glucocorticoid-dependent manner (pg. 67, 1st *pp*; as it relates to other ligand binding domains in claims 23, 31, 43, 48, 49, 51, 59, 64, 69 & 72). However, although Eilers use a human myc construct, they do not specifically teach a stable culture of human neural progenitor cells.

Evans is a review describing the well known ligand binding domains of steroid/thyroid hormone receptors (e.g., pg. 891; as it relates to estrogen, androgen, progesterone, glucocorticoid, thyroid hormone, retinoid and ecdysone receptors and their respective ligands/myc-activating chemicals in claims 23, 31, 43, 48, 49, 51, 59, 64, 69, 70 & 72). However, Evans does not teach stable cultures of human neural progenitor cells transfected with a c-myc construct.

It would have been obvious to one of ordinary skill in the art to produce stable mammalian/human neural precursor cells, as taught by Nakafuka et al., using any well known steroid/thyroid hormone receptor ligand binding domain, as taught by Evans, fused to Eilers' c-myc constructs, because Eilers et al teach that "similar chimaeras" transform cells in a steroid/ thyroid hormone-dependent manner, and because of the potential human neural stem cells specifically possess in treating neurological disease states by replacing neural tissue that no

longer exists, and by eliminating/minimizing host immuno-rejection of neural stem cells from non-human species.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert C. Hayes, Ph.D.
July 12, 2006

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER